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Editorial Comment

Threshold of Pericardial Constraint: The Pericardial Reserve Volume and Auxiliary Pericardial Functions*

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Nature has made nothing without reason

Galen

Absence of the pericardium, surgical or congenital, appears to be well tolerated. Although the cardiac contour may become more globular (1), possibly compromising the "ideal" football shape of the left ventricle, there is no obvious malfunction under rest conditions, yet the pericardium affects cardiac function under certain circumstances.

In the 1960s the *Wunderkinder* of the National Institutes of Health rediscovered and greatly expanded on the classic work of Starling on ventricular function. Since then, a few investigators have done the same with the contributions of Starling's contemporary, Yas Kuno (2), a Manchurian investigator of pericardial physiology. Many studies (3–5) in animals show that with significant volume loading the parietal pericardium has distinct effects on ventricular function and interaction that are lacking after pericardiotomy. Thus, either ventricle generates greater isovolumic pressure from any volume with the pericardium intact than in its absence. Mangano et al. (6), in this issue of the Journal, now report on comparable investigations in human beings just before coronary bypass surgery, including volume loading by straight leg raising. Over the range of pressures measured (up to 24 mm Hg in an individual subject), pericardiotomy had no apparent effect on measures reflecting systolic function (stroke work versus end-diastolic volume) and diastolic "compliance" (pulmonary wedge pressure versus end-diastolic volume). The investigations concluded that the pericardium gains hemodynamic importance only when the heart is subjected to rather high filling pressures and volumes.

Pericardial constraint. The protocol of Mangano et al. (6) is well designed and the investigation well executed; however, several considerations may limit the validity of the results. One is the generally very low range of central pressures. From the prepericardiotomy pulmonary wedge pressure of 7.5 ± 1.3 (SEM) mm Hg, one can calculate a standard deviation of 5.0, implying that relatively few patients could have had values in a higher part of the range investigated. Without more subjects with values in the higher range, the precise level at which the pericardium begins to exert hemodynamic effects (as measured by the means employed) remains uncertain. In this connection, Mangano et al. observed that, over the range measured, *"the ventricular muscle itself and not the stiffer pericardium appears to be the major determinant"* (their emphasis). The investigators could not have studied truly normal subjects and the experimental group may not have been ideal. Thirteen of the 15 patients had had one or more myocardial infarctions, implying that the myocardium was likely to be stiffer than normal and therefore less subject to pericardial influence at lower pressure-volume levels (analogous to the reduced effect of cardiac tamponade on a low compliance left or right ventricle [7]).

Pericardial constraint: potential underestimation. Although Mangano et al. (6) used reasonable indexes of systolic and diastolic performance, the negligible changes during volume loading may be a function of the sensitivity of the instruments used and the measurements investigated. For example, Smiseth et al. (8) found that open-ended catheters significantly underestimate pericardial restraint as compared with flat liquid-filled balloon catheters. Indeed, even after several holes had been made in it, the animal pericardium still exerted a constraining effect. When the pericardium was thereafter completely opened, the left ventricular diastolic pressure-diameter relation shifted markedly rightward and downward.

An indication that the level at which pericardial constraint appears may differ from the results in this study is that even small increases over normal pericardial fluid impose a marked increase in the respiratory fluctuation of systolic time intervals. As measured by blinded observers, patients with a range of apparently noncompressing pericardial effusions (none with pulsus paradoxus) showed marked respiratory fluctuations of pre-ejection period and left ventricular ejection time, significantly above those in normal subjects, patients with coronary disease and control subjects with "dry" acute pericarditis (9). Such changes were later shown (10) to be parallel with respiratory changes in echographic left ventricular size. (However, these patients had pericardial disorders, and despite the absence of tamponade, could have had a stiffer than normal pericardium.) Although Mangano et al. (6) made static observations at end-expiration (optimal timing for left ventricular function [11]), respiratory fluc-

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tuations in measurements before and after pericardiotomy might have detected differences.

Any effect of the parietal pericardium on cardiac dimensions and function must be related to the "J" shape of the pericardial pressure-volume curve (12). The flat portion of the "J" represents the period in which the " pericardial reserve volume" is depleted when the pericardial space is filling with fluid or cardiac dilation occurs. After this period, the curve ascends steeply with its "elbow" (the point of steep pressure ascent, representing pericardial constraint) arrived at sooner with more rapid intrapericardial change or with a stiffer pericardium. The essential validity of the results of Mangano et al. is not in question, but rather the level at which pericardial constraint becomes apparent. The studies of respiratory systolic interval (9) and left ventricular dimension (10) imply that the pericardial reserve volume and, consequently, the onset of pericardial constraint may be much lower than previously thought.

Disruption of the pericardium and its nonhemodynamic functions. Although "significance" in the title of the article by Mangano et al. (6) is appropriate, the work was necessarily limited to the parietal pericardium. The pericardium as a whole has considerable but poorly understood nonhemodynamic significance. Metabolic functions of the pericardial mesothelium and pericardial receptors sensitive to neural (13) and mechanical (14) stimuli have been identified. Because the mesothelium is extremely delicate, it is likely to be lost rapidly from the visceral pericardium during surgical manipulation (15). Thus, mesothelial fibrinolytic activity and production of prostacyclin and associated compounds would stop with an end to their physiologic roles (still under investigation [16,17]). For example, when applied to the epicardium of the dog, prostacyclin opposes platelet aggregation in experimentally obstructed major coronary arteries and may have a role in platelet-induced vasotonic angina (17). Moreover, the sensitivity and capacity for stimulation of pericardial mechanoreceptors (14) and neuroreceptors (18) could be different after pericardiotomy. Mangano et al. (6), of course, could not examine these aspects of removal of the pericardium, but it is an aspect that calls for further investigation when considering the "significance" of the pericardium.

Implications: pericardial protection against excessive acute dilation. The results of Mangano et al. emphasize the principal hemodynamic role of the pericardium. Evidently, up to the limit of its reserve volume, the pericardium is a mechanically relatively passive membrane. Thus, pericardial hemodynamic influence becomes apparent during such events as acute increases in cardiac volume (sharper ventricular pressure-volume relations and increased ventricular interaction) (3), acute atrioventricular valve regurgitation (perhaps limiting its extent) (19) and right ventricular infarction (right ventricular dilation tightening an otherwise lax pericardium to impose restrictive dynamics). To some degree these may protect against excessive acute increases in chamber size. As a corollary, during cardiac failure or angina (20), reduction of ventricular diastolic pressure by nitroglycerin could reflect loss of pericardial constraint when the decreased venous return shrinks cardiac volume.

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